Influence of periodic diffusive inclusions on the bidomain model

Andjela Davidovic, Yves Coudière, Clair Poignard

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Andjela Davidović[1a,2] with advisers: Yves Coudiere[1a,2,3] and Clair Poignard[1b,2]

1.Inria Bordeaux Sud-Ouest: 1a.Carmen team, 1b.MC2 team; 2.Institut de Mathematiques de Bordeaux (IBM); 3.IHU-Liryc

Introduction

We present a new mathematical model of the electric activity of the heart. The main **drawback of the standard bidomain model** is that it assumes the existence of excitable cells (myocytes) everywhere in the heart, while it is known that there exist non small regions where non-excitable cells (fibroblasts and collagen) take place. The problems that we are trying to address with our model are:

- The **laminar structure** of the myocardium that shows the presence of collagen, especially between muscle layers [2].

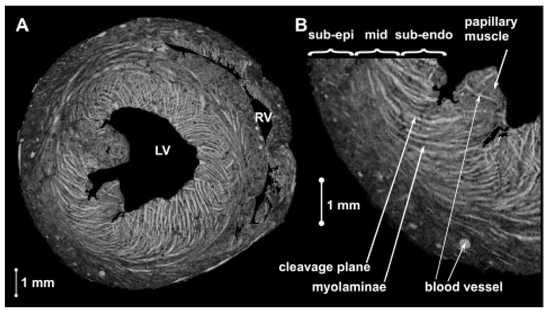


Figure 1: The laminar structure of myocardium. [3]

- The **infarct border zone**. After infraction in the heart some number of myocytes die and they are replaced by collagen and a few cells of fibroblasts. In our current model we consider as if there are no cells of fibroblasts in the extracellular space.

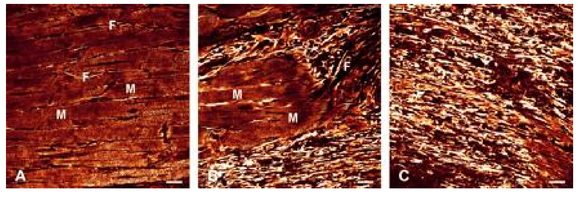


Figure 2: Fibroblast organization in sheep normal ventricular myocardium (A), infarct border zone (B) and centre (C), 1 week after infarction. [4]

I - Mesoscopic model

Modelling assumptions:

- Periodic distribution of added extracellular space
- Extracellular space is a passive conductor

Work on the domain $\Omega = B_\varepsilon \cup D_\varepsilon$

- B_ε represent the bidomain layer.
  - given intra- and extracellular conductivities σ_ε^i and σ_ε^e
  - unknown potentials u_ε^i and u_ε^e
  - define $v_\varepsilon := u_\varepsilon^i - u_\varepsilon^e$
- D_ε represent the diffusive inclusions.
  - conductivity σ_ε^d
  - unknown potential u_ε^d
- $\Sigma_\varepsilon = \partial B_\varepsilon \cap \partial D_\varepsilon$ is the interface.

The bidomain model

$$\begin{aligned} \partial_t v_\varepsilon + c v_\varepsilon &= \nabla \cdot (\sigma_\varepsilon^i \nabla u_\varepsilon^i), && B_\varepsilon, \\ \partial_t v_\varepsilon + c v_\varepsilon &= -\nabla \cdot (\sigma_\varepsilon^e \nabla u_\varepsilon^e), && B_\varepsilon, \end{aligned}$$

The diffusive inclusion

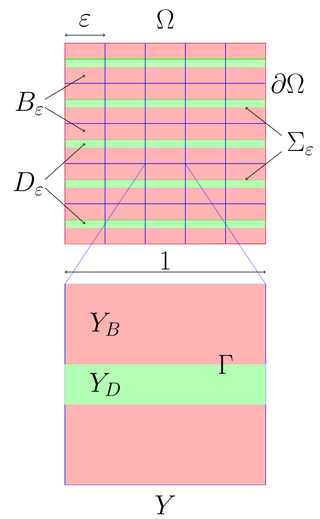
$$0 = -\nabla \cdot (\sigma_\varepsilon^d \nabla u_\varepsilon^d), \qquad D_\varepsilon,$$

The transmission conditions

$$\left.\begin{aligned} \sigma_\varepsilon^i \nabla u_\varepsilon^i \cdot n_{\Sigma_\varepsilon} &= 0, \\ \sigma_\varepsilon^e \nabla u_\varepsilon^e \cdot n_{\Sigma_\varepsilon} &= \sigma_\varepsilon^d \nabla u_\varepsilon^d \cdot n_{\Sigma_\varepsilon}, \\ u_\varepsilon^e &= u_\varepsilon^d, \end{aligned}\right| \qquad \Sigma_\varepsilon,$$

The initial and the boundary conditions given.

- We have a well posed problem up to a constant.
- Numerical simulations expensive.



II - Homogenisation

Principle: Redefine the problem in two scales and obtain the limit problem that depends only on a large scale. It gives a global, macroscopic behaviour of the unknown functions.

Assumption

$$\sigma_\varepsilon^i(x) = \sigma_i\left(\frac{x}{\varepsilon}\right), \quad \sigma_\varepsilon^e(x) = \sigma_e\left(\frac{x}{\varepsilon}\right), \quad \sigma_\varepsilon^d(x) = \sigma_d\left(\frac{x}{\varepsilon}\right).$$

Having apriori estimates on the norms of the unknown functions and their derivatives, and following the work in [1], there is a limit for $\varepsilon \to 0$

$$u_\varepsilon^i \to u_0^i, \quad u_\varepsilon^e \to u_0^e, \quad u_\varepsilon^d \to u_0^d.$$

III - Macroscopic equations

Define $\quad \sigma_i^* := \sigma_i/|Y_B|, \quad \sigma_e^* := \sigma_e/|Y_B|, \quad \sigma_d^* := \sigma_d/|Y_D|, \quad \rho = |Y_D|/|Y_B|.$

In the limit $\quad u_0^e(t,x) = u_0^d(t,x) =: u_0(t,x).$

And the limit problem is again **the bidomain model** with updated conductivities

$$\begin{aligned} \nabla_x \cdot \left((\sigma_i^* + Id)\nabla_x u_0^i\right) &= \partial_t v_0 + c v_0, \text{ in } \Omega, \\ \nabla_x \cdot \left((\sigma_e^* + \rho\sigma_d^* + (\sigma_e - \sigma_d)\,(A_e + \rho A_d))\nabla_x u_0\right) &= -(\partial_t v_0 + c v_0), \text{ in } \Omega, \end{aligned}$$

Where A_e and A_d are constant matrices that depend only on the geometry of the unit cell.

Remark:

- The modified conductivities depend on the volume fraction of the diffusive part and on the geometry of the unit cell.
- If $\sigma_e = \sigma_d$ the problem simplifies and the modified conductivities depend only on the volume fraction.

IV - Numerical verifications

We work on the numerical simulations

- On simple geometries.
- Using FEM method.
- Values of parameters obtained from the literature.
- Using *Gmsh* mesh generator ([6]) and *FreeFem++* PDE solver ([5]).

We expect to observe the convergence of the mesoscopic model to the macroscopic model.

Perspectives

We can develop our work in several directions.

- Perform numerical experiments on different geometries, simulating only the macroscopic model.
- Use real data obtained by clinicians. For example, the late enhancement MRI provides the volume fraction of the extracellular space, ρ.
- Apply the ionic current model.
- Develop a model for the infarct scar transiting from the classical bidomain, via our new model, to the purely diffusive centre of the scar.

References

[1] Allaire, *Homogenisation and two scale convergence*, SIAM J. MATH. ANAL. Vol. 23, No. 6, pp. 1482-1518, November 1992.

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Contact: andjela.davidovic@inria.fr, yves.coudiere@inria.fr, clair.poignard@inria.fr